AMENDMENTS TO THE SPECIFICATION

- On page 1, please insert the following paragraph after the title:

This application is a national stage filing under 35 U.S.C. § 371 of International Application No. PCT/EP2003/050666, filed September 29, 2003, which designated the United States and which claims priority to European Patent Application No. 02022227.9 filed October 2, 2002; the entire teachings of these referenced Applications are incorporated herein by reference. International Application PCT/EP2003/050666 was published under PCT Article 21(2) in English.

- On page 29, please replace the paragraph starting at line 9 with the following amended paragraph:

Reverse-transcription-PCR (RT-PCR) was performed using 1 μg RNA and the Omniscript® RT kit (Qiagen) using the manufacturers' recommendations. The cDNA obtained was further tested by amplifying actin cDNA using specific primers (5'-CCA GCT CAC CAT GGA TGA TG-3' (SEQ ID NO:2) and 5'-CCT TAA TGT CAC GCA CGA TTT C-3' (SEQ ID NO:3)) in order to test the quality and possible contamination with genomic DNA (to this end, RNA only is incubated in the PCR mix). cDNA was amplified by TaqMan® using the manufacturer's CyberGreen protocol and Sap-1-specific primers 5'-CAT GCT GAC CAA CTG CAT GG (SEQ ID NO: 4) and 5'-GCG AGT CCA GAG GCC AGT AA (SEQ ID NO: 5).

- On page 29, please replace the paragraph starting at line 17 with the following amended paragraph:

PCR primers for human Sap1 and GAPDH (house-keeping control) were designed using the Primer Express software from Perkin-Elmer Biosystems based on the published sequences: Sap1, reverse GCG AGT CCA GAG GCC AGT AA (SEQ ID NO: 6); forward CAT GCT GAC CAA CTG CAT GG (SEQ ID NO: 7); GAPDH, reverse GAT GGG ATT TCC ATT GAT GAC A (SEQ ID NO: 8); forward CCA CCC ATG GCA AAT TCC (SEQ ID NO: 9); intron-GAPDH, reverse CCT AGT CCC AGG GCT TTG ATT (SEQ ID NO: 10); forward CTG TGC TCC CAC TCC TGA

TTT C (SEQ ID NO:11). The specificity and the optimal primer concentration were tested on diluted series of plasmids with cDNA inserts. Potential genomic DNA (of cDNA) contamination was excluded by performing PCR reactions with specific intron-GAPDH primers. The absence of non-specific amplification was controlled by analyzing the PCR products on 3.5% agarose gels. SYBR Green Real-Time PCR reactions contained 25 µl SYBR Green PCR master mix (PE Biosystems) with 0.5 U AmpErase Uracil N-Glycosylase (UNG) and 20 µl of primers (300 nM). Template was 5 µl of RT-products; 0.5 ng total RNA from human tissues (ClonTech) or polyA+ for ovary, using PE Multiscribe enzyme). WiDr (Human Human colon adenocarcinoma, HT-29) was obtained from the ATCC. PCR was performed at 50°C for 2 min (AmpErase UNG contaminant DNA digestion; (Udaykumar et al. 1993)), 95°C for 10 min (for AmpliTaq Gold activation) and then run for 40 cycles at 95°C for 15 sec, 60°C for 1 min on the ABI PRISM 7700 Detection System. The reverse-transcribed cDNA samples were thus amplified and their Ct (cycle threshold) values were determined. All Ct values were normalized to the housekeeping gene GAPDH. A single specific DNA band for human Sap1and GAPDH was observed using gel electrophoresis analysis.

- On page 30, please replace the paragraph starting at line 7 with the following amended paragraph:

The peptides tested corresponded to src (TSTEPQ**Z**QPGENL (SEQ ID NO: 12); **Z** = phosphotyrosine) and lck (FFTATE.G.Q**Z**QPQP (SEQ ID NO: 13)) C-terminal sequences; both were purchased from Neosystems. The GST-PTP enzymes were made and tested using Malachite Green as an indicator for free phosphate as described earlier (Wälchli et al. 2000). Per assay 1.25 ng of PTP was tested with 200 µM phosphopeptide in 40 µl that also contained 50 mM HEPES pH 7.2, 1 mM EDTA, 1 mM DTT and 0.05% (v/v/) NP-40. After incubation (30 min. at room T) 100 µl BioMol Green (BioMol) was added, and after a further 20 min the OD_{650} was measured. The OD was converted to free nmoles phosphate using a standard curve.

- On page 30, please replace the paragraph starting at line 31 with the following amended paragraph:

The PTP-Sap1 FL construct (Matozaki et al. 1994) was subcloned into several vectors using *Xba*I and *Hin*dIII restriction enzymes into the pcDNA4a vector (Invitrogene). The pcDNA4-Sap1intra HA clone is a fusion of the signal peptide sequence of PTP-Sap1, followed by a HA-tag and the PTP sequence from the N-terminal part of the TM. It was prepared as follows: the full cytoplasmic domain of PTP-sap1 was amplified by PCR (polymerase chain reaction) using Herculase Polymerase (Stratagene) and an antisense primer from the vector and a sense primer containing the HA-tag fused to the sequence encoding the five extracellular amino acids on the N-terminal side of the TM (5'-TAC CCA TAC GAC GTC CCA GAC TAC GCT CAC ACC GAG AGT GCA GGG GT-3') (SEQ ID NO: 14). From the other end, the signal peptide was amplified with a reverse primer fused to the HA-tag in the C-terminal part of the sequence (5'-AGC GTA GTC TGG GAC GTC GTA TGG GTA GGG GGC AGG CGC CCT GGC CCC T-3') (SEQ ID NO: 15) and the forward primer was from the vector. The two PCR products were mixed and amplified again with external primers. Two *Xba*I sites (one generated and the other one from the original vector) surrounding the amplicon were used to insert the intracellular part of PTP-Sap1 fused to the signal peptide and the HA-tag. The full length construct fused in C-terminal with an HA-tag was prepared with an antisense primer containing the sequence of a *Xho*I site, an HA-tag and the end of the PTP-Sap1 sequence with the STOP codon (5'-TAC TCG AGT TAA GCG TAG TCT GGG ACG TCG TAT GGG TAG ACC TCC AAC TTG TGG GCC T-3') (SEQ ID NO: 16). The full length Sap1-HA fusion construct was amplified using a plasmid specific forward primer in a long run PCR using Herculase in the presence of 5% DMSO and "hotstart" conditions. The HA-tag construct in N-terminal could never be obtained. FLEX construct was obtained by amplifying the ECD sequence with a primer complementary to the intracellular proximal TM coding sequence (about 30 bp down stream) in order to keep the targeting sequence (5'-ATG AAT TCA GCG GCC CAT CTG GCT GCC TCT TTC TCA GGA AGA AAA TCA-3') (SEQ ID NO: 17) and adding an *Eco*RI site. When the amplicon is fused to pCDNA4b, it is in frame with the two tags (His and c-Myc) and a stopcodon. The C- and the N-terminal deletion in FLEX were performed by digestion of the pcDNA4-FLEX construct using ECD coding sequence cutting enzymes that maintain the correct reading frame. XcmI (NEB) and PstI were used to digest pcDNA4-FLEX; the larger fragments (containing the truncated FLEX) were purified and ligated again, for C- and N-terminal constructs,

respectively. The GST-Sap1 construction was described previously (Wälchli et al. 2000). PTP-Sap1 ma (membrane associated) consists of the fusion of the PTP-Sap1 cytoplasmic region with a HA-tag in its C-terminal part (amplification from the pcDNA4-PTP-Sap1FLHA construct). A primer containing the Lck myristilation site (underlined) and a start codon surrounded by a Kozak sequence ATA AGC TTA CCA TGG GCT GTG GCT GCA GCT CAC ACC CGG AAG ATG ACT GGA AGA GGA GGA ATA AGA AGA AG (SEQ ID NO: 18), was used with a vector primer to amplify the cytoplasmic fragment of PTP-Sap1. The amplicon was cloned into pcDNA4 using *Hin*dIII restriction site of the primer for the 5' end ligation.

- On page 32, please replace the paragraph starting at line 3 with the following amended paragraph:

Site-directed mutagenesis. The exchange of (a) codon(s) was done as follows. PCR was performed with Pfu Polymerase (Promega) following a special program with an extension time relative to the size of the plasmid used (0.5 kb/minute) for 14 cycles. Following the amplification of 100 ng of plasmid, DpnI is incubated in the mix for 1 hour at 37°C. Ultracompetent cells (XL2-blue, Stratagene) were transformed with 1/10 of the PCR mix and plated in selective medium. For PTP-Sap1 site-directed mutagenesis, the pair of primers was the following: C747S (5'-CTC TGT GGT CAG CCA CAC CGA GAG T-3' (SEQ ID NO: 19) and 5'- CTC GGT GTG GCT GAC CAC AGA GTG A -3') (SEQ ID NO: 20), D986A (trapping mutant, 3'- GCC TGG CCG GCT CAC GGC GTT CCC T -5' (SEQ ID NO: 21) and 3'- AAC GCC GTG AGC CGG CCA GG -5') (SEQ ID NO: 22), Y1094F (3'-CGA GAA GGA AGT CCC GTT TGA GGA T-5' (SEQ ID NO: 23) and 3'-CAT CCT CAA ACG GGA CTT CCT TCT C-5') (SEQ ID NO: 24), Y1002F (3'-TGT CGA AAA CCT CAT CTT CGA GAA C-5'(SEQ ID NO: 25) and 3'-CGG CCA CGT TCT CGA AGA TGA GGT T-5') (SEQ ID NO: 26).

- On page 32, please replace the paragraph starting at line 18 with the following amended paragraph:

c-Src cDNA was cloned in different vectors, but mostly used in pcDNA4. The c-Src Y530F mutant was made using the method previously described with the following primers (5'-AGT TCC

AGC CCG GGG AGA ACC TC -3' (SEQ ID NO: 27) and 5'- GAG GTT CTC CCC GGG CTG GAA CT-3' (SEQ ID NO: 28)).

- On page 35, please replace the paragraph starting at line 18 with the following amended paragraph:

In the process of construction full-length Sap-1 expression vectors sequencing, errors were corrected in the previously published sequence. Fig. 1A shows the corrected, full-length Sap-1 amino acid sequence (SEQ ID NO: 1). Fig. 1B shows an overview over the different Sap-1 recombinant proteins that were used in the present examples.

- On page 39, please replace the paragraph starting at line 29 with the following amended paragraph:

The sequences of the primers were (AS: antisense, S: scramble): AS1: CCA GCC ATG CCT CCA GAC ACT (SEQ ID NO: 29), S1: TGC CCA CAC TCA AGC ACC CTG, AS2 (SEQ ID NO: 30): TGA CCC GGG TCC AAG GCC AT (SEQ ID NO: 31), S2: GCG CGC TAG CCA CTT CGG AA (SEQ ID NO: 32), AS3: TGG TGT CTG TTG TGT TTC GA (SEQ ID NO: 33), S3: AGG GTC GGT TTT TTG GTT CT (SEQ ID NO: 34).

- Please insert the Abstract, appearing on the next page, immediately after the last page of the claims.